

REMARKS

The Office Action mailed March 5, 2003 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendments. Support for the amendments to the claims can be found throughout the specification as originally filed. For example, support for the amendments may be found on page 14, line 15 through page 16, line 21; page 19, lines 20-23; page 23, line 1 through page 25, line 29; and page 25, line 31 to page 26, line 19.

Specification

Applicants acknowledge, with appreciation, the indication made on the Office Action Summary sheet mailed with the Office Action of March 5, 2003 that the formal drawings filed June 29, 2001 are accepted.

Status of the Claims

Upon entry of the foregoing amendment, claims 25-44 will be pending.

Priority

The Office Action at page 2 indicates that if Applicants desire to make a priority claim based on a previously filed copending application, specific reference to the earlier filed application must be made in the application. Applicants filed a preliminary amendment on February 6, 2001 to recite the priority claim before the first sentence of the application. Entry of the amendment is requested.

The Rejection of Claims 25-27, 30-37, 39 and 42 under 35 U.S.C. § 102(e) as being Allegedly Anticipated by U.S. Patent 6,054,270 to Southern et al.

Claims 25-27, 30-37, 39 and 42 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent 6,054,270 to Southern *et al.*

Applicants respectfully traverse the rejection because the '270 patent does not teach or suggest the limitations present in the claims.

The pending claims are directed to a method of detecting a mutation in a target nucleic acid sequence *versus* a known sequence.

Contrary to the allegations made in the Office Action, the '270 patent does not teach the presently claimed methods because nowhere in the '270 patent is there any teaching or suggestion of known core sequence probes, determining binding affinity or comparing the binding affinity of a known core sequence probe to a target sequence and a known sequence.

The Office Action mailed March 5, 2003 at page 4, lines 2-4 quotes a portion of the '270 patent and cites the whole document, especially the abstract and Example 3. The quote reads “ ‘array with multiple oligonucleotides including 19mer oligonucleotide compare hybridization affinity against a temperature gradient thereby detecting mismatches.’ ” Applicants have carefully reviewed the whole '270 patent and are unable to locate this quote. In fact, an electronic search of the '270 patent as it exists on the USPTO website has been unable to locate any recitation of the words “affinity”, “affinities” or “gradient” anywhere in the '270 document. Applicants respectfully request that the Office point to where in the '270 patent any mention is made of binding affinity or absolute binding affinity.

The Office Action asserts at page 4, lines 9-10 that the terms “core sequence probe” and “absolute binding affinity” read broadly on the array probes and measurement of hybridization targets disclosed in the '270 patent. Applicants respectfully disagree. The known core sequence probes of the instant invention are not taught in the '270 patent because nowhere does the '270 patent teach sequences that are expected to be exactly complementary to a target sequence to detect a mutation in the target nucleic acid sequence versus a known sequence.

Furthermore, Applicants respectfully assert that “measurement of resulting hybridization targets,” which the Office Action alleges is taught in the '270 patent, is not the same as determining binding affinity, which is what is required by the instant claims. This is because the method of the '270 patent relies on detecting only perfectly matched sequences to targets. See, for example column 10, lines 12-13 stating that “[n]o signal was detectable on the patch with the mismatched sequence.” See also column 10, lines 59-61 stating “only the perfectly matched 19-mer was stable, all other oligonucleotides had been eluted.” See also column 10, lines 63 to

column 11, line 2 stating “[m]ismatches at the end of the oligonucleotides and at internal sites can all be melted under conditions where the perfect duplex remains. Thus we are able to use very stringent hybridisation conditions that eliminate annealing to mismatch sequences or to oligonucleotides differing in length by as little as one base.” See also column 11, lines 30-35 stating “mismatches considerably reduced the melting temperatures of the hybrids, and conditions were readily found such that the perfectly matched duplex remained whereas the mismatched duplexes had fully melted.” There is no comparison of binding affinities made in the ‘270 patent because only perfectly matched sequences are detected.

Thus, the ‘270 patent does not teach determining binding affinity because the method relies entirely on eliminating binding of mismatched sequences. Neither does the ‘270 patent teach comparison of binding affinities because only perfectly matched sequences are detected. Furthermore, the ‘270 patent does not teach or suggest “known core sequence probes.” For these reasons, withdrawal of the rejection is respectfully requested.

The Rejection of Claim 38 under 35 U.S.C. § 103(a) as being Unpatentable over U.S. Patent 6,054,270 to Southern et al. in view of U.S. Patent 5,633,137 to Shuber

The Office Action alleges that the claim 38 is obvious over the combination of the ‘270 patent and the ‘137 patent for the reasons *supra* and because the ‘137 patent discloses ASO probes for detection of mutations in P-53.

Applicants incorporate by reference the comments made above with respect to the ‘270 patent. Respectfully, the ‘137 patent does not cure these deficiencies.

The Rejection of Claims 40 and 41 under 35 U.S.C. § 103(a) as being Unpatentable over U.S. Patent 6,054,270 to Southern et al. in view of U.S. Patent 4,965,189 to Owerbach

The Office Action alleges that the claims 40 and 41 are obvious over the combination of the ‘270 patent and the ‘189 patent for the reasons *supra* and because the ‘189 patent discloses probes for detection of mutations in DQ beta gene.

Applicants incorporate by reference the comments made above with respect to the ‘270 patent. Respectfully, the ‘189 patent does not cure these deficiencies.

The Rejection of Claim 43 under 35 U.S.C. § 103(a) as being Unpatentable over U.S. Patent 6,054,270 to Southern et al. in view of U.S. Patent 5,468,613 to Erlich et al.

The Office Action alleges that the claim 43 is obvious over the combination of the '270 patent and the '613 patent for the reasons *supra* and because the '613 patent discloses probe hybridization in forensic analysis.

Applicants incorporate by reference the comments made above with respect to the '270 patent. Respectfully, the '613 patent does not cure these deficiencies.

The Rejection of Claims 28 and 29 under 35 U.S.C. § 103(a) as being Unpatentable over U.S. Patent 6,054,270 to Southern et al. in view of U.S. Patent 5,324,633 to Fodor et al.

The Office Action alleges that the claims 28 and 29 are obvious over the combination of the '270 patent and the '633 patent for the reasons *supra* and because the '633 patent discloses plotting the binding affinity results of fluorescence assays on graph and normalized [sic].

Applicants incorporate by reference the comments made above with respect to the '270 patent. Respectfully, the '633 patent does not cure these deficiencies because it is directed to ligand receptor interactions.

Conclusion

In view of the foregoing amendments and response, the Applicants respectfully request withdrawal of the outstanding rejections and early notice of allowance to that effect.

If the Examiner finds that a telephone conference would further prosecution of this application, he is invited to call the undersigned at his convenience.

EXCEPT for issue fees payable under 37 C.F.R. §1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP



Michael S. Tuscan
Reg. No. 43,210

Dated: June 5, 2003

Customer No. 000033522
Morgan, Lewis & Bockius LLP
1111 Pennsylvania Avenue, NW
Washington, DC 20004
(202) 739-3000
(202) 739-3101 - fax